

Amendments to the Claims

Please cancel claims 1-11 without prejudice or disclaimer of the subject matter therein. Amend claims 12 and 22-28; and add new claims 30-47 as follows:

1. (canceled)
2. (canceled)
3. (canceled)
4. (canceled)
5. (canceled)
6. (canceled)
7. (canceled)
8. (canceled)
9. (canceled)
10. (canceled)
11. (canceled)

12. (withdrawn; currently amended) A method for inhibiting expression of a selected protein by a large circular single-stranded nucleic acid molecule targeted to an RNA encoding the selected protein comprising, ~~targeting the nucleic acid molecule to the RNA such that the nucleic acid molecule hybridizes with the RNA to form a duplex with the RNA, wherein the duplex inhibits expression of the selected protein~~ contacting a cell expressing the protein with the composition according to claim 36, which is targeted for the protein.

13. (withdrawn) The method according to claim 12, wherein expression of said target protein causes cell proliferation or cancer.

14. (withdrawn) The method according to claim 13, wherein said cancer is leukemia, lung cancer, liver cancer, colon cancer, stomach cancer, pancreatic cancer, brain cancer or prostate malignancy.

15. (withdrawn) The method according to claim 14, wherein said cancer is leukemia, cervical cancer, or breast cancer.
16. (withdrawn) The method according to claim 13, wherein said target protein is tumor necrosis factor, nuclear factor, MYB, MYC, RAS, or cell division kinase.
17. (withdrawn) The method according to claim 12, wherein said protein is a viral protein.
18. (withdrawn) The method according to claim 17, wherein said virus is herpes, human papilloma virus (HPV), HIV, small pox, mononucleosis (Epstein-Barr virus), hepatitis, or respiratory syncytial virus (RSV).
19. (withdrawn) The method according to claim 12, wherein expression of said target protein causes a metabolic disease or an immunological disorder.
20. (withdrawn) The method according to claim 19, wherein said metabolic disease is phenylketonuria (PKU), primary hypothyroidism, galactosemia, abnormal hemoglobins, types I and II diabetes, or obesity.
21. (withdrawn) The method according to claim 18, wherein said immunological disorder is Sjogren's Syndrome, antiphospholipid syndrome, immune complex diseases, Purpura, Schoenlein-Henoch, immunologic deficiency syndromes, systemic lupus erythematosus, immunodeficiency, rheumatism, kidney, or liver sclerosis.
22. (currently amended) A chimeric large circular single-stranded nucleic acid molecule comprising a plurality of target-specific antisense regions, ~~which specifically bind to a plurality of target RNA expressed from a plurality of target genes~~, wherein said nucleic acid molecule is effective for reducing the expression of said genes, wherein the molecule is at least about 3,000 nucleotides long.

23. (currently amended) A composition comprising a chimeric large circular single-stranded nucleic acid molecule comprising a plurality of target-specific antisense regions, which ~~specifically bind to a plurality of target RNA expressed from~~ are specific for a plurality of target genes, wherein said nucleic acid molecule is effective for reducing the expression of said genes, and a pharmaceutically acceptable carrier thereof.

24. (withdrawn; currently amended) A method for inhibiting expression of a plurality of selected proteins ~~by a large circular nucleic acid molecule targeted to a plurality of RNA molecules encoding a plurality of selected proteins comprising,~~

(i) ~~generating a chimeric large circular nucleic acid molecule comprising target-specific antisense regions targeted to said plurality of target RNA; and~~

(ii) ~~targeting the plurality of RNA such that the chimeric large circular nucleic acid molecule hybridizes with said RNA to form a duplex, wherein the duplex reduces expression of the plurality of selected proteins~~ comprising contacting a cell expressing the proteins with the target-specific composition according to claim 36.

25. (withdrawn; currently amended) A method for inhibiting cell proliferation, comprising,

~~administering to said cell, a large circular nucleic acid molecule that comprises one or more antisense region substantially complementary to one or more target gene, the composition according to claim 30,~~ in which inhibiting expression of ~~said~~ a target gene or genes inhibits cell proliferation.

26. (withdrawn; currently amended) A method of making a the large circular single-stranded nucleic acid molecule comprising target-specific antisense region according to claim 30, which inhibits expression of a ~~selected~~ protein, comprising,

(i) inserting a target-specific DNA of interest into a phage or phagemid genome;

(ii) allowing the phage to generate a single stranded form, which is the large circular nucleic acid molecule; and

(iii) isolating said large circular nucleic acid molecule ~~by gel filtration column.~~

27. (withdrawn; currently amended) A method of screening for a function of a gene comprising,
- (a) generating a large circular single-stranded nucleic acid molecule comprising ~~an~~ a target-specific antisense region ~~that is substantially complementary to an RNA expressed from a cell;~~
 - (b) contacting a the cell with the ~~large circular nucleic acid molecule~~ composition according to claim 30, such that the ~~antisense~~ molecule enters the cell and hybridizes to an RNA expressed in the cell to inhibit expression of its gene product; and
 - (c) assaying the cell for a variation of a phenotype.
28. (withdrawn) The method according to claim 27, wherein steps (a) to (c) are applied to a library of said large circular single-stranded nucleic acid molecule.
29. (withdrawn) The method according to claim 27, wherein said nucleic acid molecule is a single stranded form of a recombinant bacteriophage or phagemid genome.
30. (new) A composition comprising:
- (i) a large circular single-stranded nucleic acid molecule comprising at least one target-specific antisense region, wherein said large circular single-stranded nucleic acid molecule is effective for reducing expression of said gene, wherein said molecule is at least about 3,000 nucleotides long; and
 - (ii) a transfection effective carrier thereof.
31. (new) The composition according to claim 30, wherein the antisense region of the molecule is at least about 50 nucleotides long.
32. (new) The composition according to claim 30, wherein the antisense region is complementary to an entire gene sequence.

33. (new) The composition according to claim 30, wherein the nucleic acid molecule is a single stranded recombinant bacteriophage or phagemid genome.
34. (new) The composition according to claim 30, wherein said bacteriophage or phagemid is a filamentous phage.
35. (new) The composition according to claim 34, wherein the filamentous phage is phage M13.
36. (new) A composition comprising:
- (i) a large circular single-stranded nucleic acid molecule comprising at least one target-specific antisense region, wherein said large circular single-stranded nucleic acid molecule is effective for reducing expression of said gene, wherein said molecule comprises a recombinant bacteriophage or phagemid genome; and
 - (ii) a transfection effective carrier thereof.
37. (new) The composition according to claim 36, wherein the antisense region of the molecule is at least about 50 nucleotides long.
38. (new) The composition according to claim 36, wherein the antisense region is complementary to an entire gene sequence.
39. (new) The composition according to claim 36, wherein the molecule is at least about 3,000 nucleotides long.
40. (withdrawn; new) A method for inhibiting expression of a protein by a large circular single-stranded nucleic acid molecule targeted to an RNA encoding the selected protein comprising contacting a cell expressing the protein with the composition according to claim 30, which is targeted for the protein.

41. (new) A chimeric large circular single-stranded nucleic acid molecule comprising a plurality of target-specific antisense regions, wherein said nucleic acid molecule is effective for reducing expression of said genes, wherein said molecule comprises a recombinant bacteriophage or phagemid genome.
42. (new) A composition comprising a chimeric large circular single-stranded nucleic acid molecule comprising a plurality of target-specific antisense regions, wherein said nucleic acid molecule is effective for reducing expression of said genes, and a pharmaceutically acceptable carrier thereof.
43. (withdrawn; new) A method for inhibiting expression of a plurality of proteins comprising contacting a cell expressing the proteins with the target-specific composition according to claim 30.
44. (withdrawn; new) A method for inhibiting cell proliferation comprising administering to said cell the composition according to claim 30, in which inhibiting expression of a target gene or genes inhibits cell proliferation.
45. (withdrawn; new) A method of screening for a function of a gene comprising,
(a) generating a large circular single-stranded nucleic acid molecule comprising at least one target-specific antisense region;
(b) contacting the cell with the composition according to claim 36, such that the molecule enters the cell and hybridizes to an RNA expressed in the cell to inhibit expression of its gene product; and
(c) assaying the cell for a variation of a phenotype.
46. (new) The composition according to claim 30, wherein the transfection effective carrier is liposome.
47. (new) The composition according to claim 36, wherein the transfection effective carrier is liposome.